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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER |
|---|
| RAO, MANJUNATH N |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | 17 |

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/087,775 | INABA ET AL. | |
| | Examiner | Art Unit | |
| | Manjunath N. Rao, Ph.D. | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *9-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

Claims 1-15 are currently pending in this application.

### *Election/Restrictions*

Applicant's election without traverse of Group I, claims 1-8 in Paper No. 10 is acknowledged.

### *Priority*

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). However, Examiner notes that applicants have not provided a translation of the Japanese language document.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-8 recite the term "gene". The metes and bounds of the above term in the context of the above claims are not clear to the Examiner. Examiner suggests applicants to use the term "polynucleotide" in place of the term "gene".

Claim 1 and claims 2-8 which depend from claim 1 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is drawn to a method of producing a protein by introducing a recombinant vector "in which a fusion gene encoding a protein constituting a virus particle and a gene encoding a desired protein are incorporated". However, the above phrase does not explicitly indicate that the encoded viral protein and the desired protein are encoded as a fusion protein rendering the claim indefinite. Correction is required.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites the phrase "down stream". It is not clear to the Examiner as to what applicants mean by the above phrase in the context of the above claim. More specifically it appears that applicants intend to mean "located towards the C-terminal of gp64 protein". If this is so, amending the claim accordingly would overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a protein of a specific size (i.e., medium to low molecular size proteins that can be fit in to the viral gene) comprising the steps of introducing

into a insect cell, a recombinant vector encoding a fusion protein, wherein the fusion protein comprises a coat protein of a baculovirus fused to a desired protein, wherein expression of the fusion protein in said host cell produces the desired protein fused with said virus particle, does not reasonably provide enablement for such a method to produce any or all type of proteins using any or all host cells or any or all proteins constituting any or all virus particles. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-8 are so broad as to encompass a method of making a protein by a phage display technique using any or all host cells or any or all proteins constituting any or all virus particles. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of host cells, virus proteins and viral particles broadly encompassed by the claims. It is well know in the art that not all any type of host cells can be used for expression of the virus. Only host cells that are sensitive or succumb to the said virus can be used for the above purposes. On similar lines, it also well known that not all viral proteins or all virus particles are suitable for the above method. The most preferred virus are the phage type virus which are lethal to host cells only and not to those operators who

actually culture the virus. The question of lethality to humans plays a clear role in selecting the type of virus. Furthermore, it is also well known in the art that only DNA encoding virus coat proteins are capable of taking on added sequences encoding the desired protein of only certain specific sizes can be produced by this type of "phage display method" and not all or any size/type of protein is suitable for the above method. Since all the above factors, i.e., size and type of desired protein, host cell, virus coat protein, and type of virus determine the specific type of protein and a specific method of making the protein, those skilled in the art requires a knowledge of and guidance with regard to which type of host cell, types of protein to be made, type of virus to be used etc. and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the method of making a specific glycosyltransferase using an insect cell lines as a host cell and a baculovirus as the virus with its coat protein gp64 for making the fusion protein. It would require undue experimentation of the skilled artisan to make and use the claimed method. The specification is limited to teaching the use of baculovirus gp64 and insect cell line sf6 as host cells for making a glycosyltransferase. In view of the great breadth of the claim, amount of experimentation required to make the method work, the lack of guidance, working examples, and unpredictability of the art in predicting function from a primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a

reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all or any type of protein, host cells, viral protein and viral particles because the specification does not establish: (A)all or any type of proteins can be made by the above methods; (B) that all or any type of host cell can be used for the above method; (C) that all or any viral particles can be used for the above method, (D) that all or any viral protein can be used for making the fusion protein.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all or any host cell, proteins, viral proteins and virus particles with an enormous number of amino acid modifications as well. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the above method having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8 are directed to method of making polypeptides using a phage display technique. Claims 1-8 are rejected under this section of 35 USC 112 because the claims are directed to a method of making a genus of polypeptides including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue (i.e., those polypeptides that are to be made as well as the viral peptide that will be used for fusion). No description has been provided of the polypeptide sequences encompassed by the claim. No information, has been provided by applicants which would indicate that they had possession of the claimed genus of polypeptides. The specification does not contain any disclosure of the structure or function of all the polypeptide sequences within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structure/functions. Therefore many structurally and functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Mottershead et al. (BBRC, 1997, Vol. 238:717-722) or Boublik et al. (Biotechnology, 1995, Vol. 13:1079-1084 or Grabherr et al. (Biotechniques, 1997, Vol. 22(4):730-737). This rejection is based upon the public availability of a printed publication more than one year before the filing date of the instant application. Claims 1-5 of the instant application is drawn to a method of producing a protein of comprising the steps of introducing into a host cell such as an insect cell, a recombinant vector encoding a fusion protein, wherein the fusion protein comprises a coat protein of a baculovirus such as gp64 fused to a desired protein, wherein expression of the fusion protein in said host cell produces the desired protein fused with said virus particle and is displayed on the virus particle and wherein the desired protein thus produced is purified. All the above three references disclose such an identical method using the insect cell line sf6. Therefore, Mottershead et al., Boublik et al. and Grabherr et al. anticipate claims 1-5 as written.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mottershead et al. or Boublik et al. or Grabherr et al as applied to claims 1-5 above, and further

in view of the common knowledge in the art of protein biochemistry and molecular biology. Claims 7 and 8 are drawn to a method of making a glycosyltransferase using the phage display technique of claims 1-5 and further purifying the desired protein by cleaving the protein from the viral coat protein or virus particle.

The references of Mottershead et al., Boublik et al. and Grabherr et al. have already been discussed above. The above reference actually teach and suggest that any type of desired protein can be produced using the baculovirus system. In that context, one of the reference also teaches that a commercial kit is available for producing recombinant proteins. Therefore, using the teachings and suggestions of the above reference it would have been obvious to those skilled in the art to make any protein or specifically any glycosyltransferase using that above method. Polynucleotides encoding many glycosyltransferase are available in the art. Using such polynucleotides and the methods taught by the above three references it would have been obvious to those skilled in the art to introduce a protease cleavage site in the fusion protein and a tag such as GST of His tag such that the protein can be easily cleaved from the viral particle followed by affinity purification. One of ordinary skill in the art would have been motivated to do so as the method offers several advantages such as bulk culture technique for large scale production, easy purification of the recombinant protein etc. One of ordinary skill in the art would have a reasonable expectation of success since the above reference provide all the required steps for the method and polynucleotides encoding glycosyltransferase are available in the art.

Therefore the above invention would have been *prima facie* obvious to those skilled in the art.

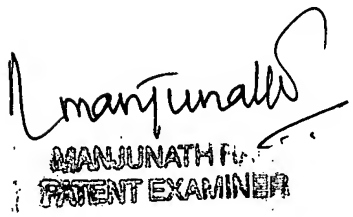
***Conclusion***

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.




Manjunath N. Rao
September 10, 2003